

## REMARKS

Claims 1-5, 7-16, 18-36 and 52-70 are pending and are under examination. The specification has been amended as requested by the Examiner to delete an embedded hyperlink. Claim 1 has been amended to merely correct a typographical error. Accordingly, these amendments do not raise an issue of new matter and entry thereof is respectfully requested.

### Objection to the Disclosure

The specification has been objected to for containing an embedded hyperlink on page 32, line 26. The specification has been amended as suggested by the Examiner, and the objection to the specification is respectfully requested to be withdrawn.

### Rejections Under 35 U.S.C. § 103

The rejection of claims 1, 2, 4, 5, 12, 24, 25, 27, 33-36, 52-57, 59, 60 and 66-70 under 35 U.S.C. § 103 as allegedly obvious over Yates, J. Mass Spectrom. 33:1-19 (1998) is respectfully traversed. Applicant respectfully maintains that these claims are unobvious over Yates.

In the Office Action on page 3, it is asserted that the specification indicates that “absence of ion selection” refers to “all ions being fragmented at the source followed by simultaneous mass spectrometer analysis, such that all ions (i.e. subset of parent polypeptides) are subjected to the mass spectrometer.” The Office Action further indicates that “several polypeptides” refers to “all polypeptides.” While several polypeptides can refer to all polypeptides, the specification teaches that simultaneous determination of the mass of a subset of polypeptides can be performed in the absence of ion selection of a single ion for mass determination and that several polypeptides can be selected rather than a single ion (page 55, lines 8-12). The specification further teaches that simultaneous determination of masses of a subset of polypeptides can be performed in the absence of single ion selection or in the absence of ion selection in a source region (page 55, lines 18-21). Therefore, it is

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respectfully submitted that “absence of ion selection” refers to absence of single ion selection or absence of ion selection in a source region, which can include, but does not require, selection of all polypeptides.

With regard to the assertion in the Office Action that the specification indicates the limitation “absence of ion selection” as “all ions being fragmented at the source followed by simultaneous mass spectrometer analysis,” Applicant points out, as discussed above, that the specification teaches that “absence of ion selection” refers to absence of single ion selection or absence of ion selection in a source region. However, the specification does not teach, as asserted in the Office Action, that “absence of ion selection” means that all ions are fragmented at the source. For example, Figure 2B exemplifies fragmentation occurring in the collision cell. Therefore, in contrast to the assertion in the Office Action, the phrase “absence of ion selection” does not mean that all ions are necessarily being fragmented at the source.

Applicant respectfully maintains, for the reasons of record, that Yates does not teach or suggest the claimed methods. In particular, Yates does not teach or suggest a method of identifying a polypeptide by simultaneously determining the mass of a subset of parent polypeptides from a population of polypeptides and the mass of fragments of the subset of parent polypeptides, as recited in claim 1. In addition, Yates does not teach or suggest a method of identifying a polypeptide where the fragment mass is determined by mass spectrometry in the absence of ion selection for producing fragment ions, as recited in claims 13, 24 and 56.

In corroboration of Applicant’s assertion that Yates does not teach or suggest the claimed invention, submitted herewith is a Rule 132 Declaration by Dr. Goodlett (Exhibit A). In the Declaration, Dr. Goodlett attests that the historical mass spectrometry methods described by Yates are distinct from the claimed methods. It is respectfully submitted that the Declaration by Dr. Goodlett corroborates Applicant’s position that Yates does not teach or suggest the claimed methods where the mass of a subset of parent polypeptides from a population are measured simultaneously with the mass of fragments of the subset of parent

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polypeptides or where the fragment mass is determined by mass spectrometry in the absence of ion selection for producing fragment ions.

Furthermore, Applicant respectfully maintains, for the reasons of record, that Yates does not teach or suggest the use of an annotated polypeptide index. Applicant respectfully disagrees with the assertion in the Office Action on page 4 that it would have been obvious to use an annotated polypeptide index of predicted values and empirically determined values. The passage in Yates referenced in the Office Action lies in the following context:

The observed  $m/z$  values are compared with the values predicted after digestion of each protein in the database with a site specific enzyme (Fig. 3). Provided a sufficient number of peptide ions are observed in the mass analysis step, and the protein is not heavily modified, and there are not more than two proteins present, a match can generally be found. This method has found significant application in the rapid identification of proteins from gels, in particular, in the identification of proteins from two-dimensional gels.<sup>84</sup> A level of uncertainty in the identification can be observed when searching large databases with this technique, consequently it [this technique] has been combined with other types of information to increase the specificity of the identification.

Yates, paragraph bridging pages 7-8. As indicated above, it is respectfully submitted that “it” refers to “this technique,” peptide mass mapping by mass spectrometry, not databases, as asserted in the Office Action. Applicant respectfully maintains that Yates does not teach or suggest the use of an annotated polypeptide index comprising at least one empirically determined characteristic for each of the polypeptides in the index.

As discussed above, Applicant maintains that the claimed methods are unobvious over Yates. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1-5, 12-16, 23-27, 33-36, 48-60 and 66-70 under 35 U.S.C. § 103 as allegedly obvious over Yates, *supra*, in view of Gygi et al., Nat. Biotechnol. 17:994-999 (1999), is respectfully traversed. Applicant respectfully maintains that these claims are unobvious over Yates, alone or in combination with Gygi et al.

As discussed above and corroborated by Dr. Goodlett's Declaration, Applicant respectfully maintains that Yates does not teach or suggest the claimed methods. Furthermore, Gygi et al. does not cure the deficiencies of the primary reference. Therefore, Applicant respectfully maintains that Yates, alone or in combination with Gygi et al., cannot render the claimed methods obvious. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

The rejection of claims 1-5, 7-16, 18-36 and 52-70 under 35 U.S.C. § 103 as allegedly obvious over Yates, *supra*, in view of Gygi et al., *supra*, and further in view of Easterling et al., Anal. Chem. 71:624-632 (1999), is respectfully traversed. Applicant respectfully maintains that these claims are unobvious over Yates, alone or in combination with Gygi et al. and/or Easterling et al.

As discussed above and corroborated by Dr. Goodlett's Declaration, Applicant respectfully maintains that Yates does not teach or suggest the claimed methods. Furthermore, neither of Gygi et al. nor Easterling et al. can cure the deficiencies of the primary reference. Therefore, Applicant respectfully maintains that Yates, alone or in combination with Gygi et al. and/or Easterling et al., cannot render the claimed methods obvious. Accordingly, Applicant respectfully requests that this rejection be withdrawn.

### CONCLUSION

In light of the amendments and remarks herein, Applicant submits that the claims are now in condition for allowance and respectfully requests a notice to this effect. The Examiner is invited to call the undersigned agent if there are any questions.

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To the extent necessary, a petition for an extension of time under 37 C.F.R. 1.136 is hereby made. Please charge any shortage in fees due in connection with the filing of this paper, including extension of time fees, to Deposit Account 502624 and please credit any excess fees to such deposit account.

Respectfully submitted,

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A handwritten signature in cursive script, appearing to read "Deborah L. Cadena".

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